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Palladium-catalyzed direct desulfitative C2 arylations of 3-halo-*N*-protected indoles using (hetero)arenesulfonyl chlorides

Anoir Hfaiedh,^{a, b, c} Hamed Ben Ammar,^b Jean-François Soulé,^{a*} and Henri Doucet^{a*}

The direct arylation of *N*-protected 3-haloindole derivatives with benzenesulfonyl chlorides as coupling partners using 5 mol% of bis(acetonitrile)dichloropalladium(II) catalyst and lithium carbonate as base in 1,4-dioxane was investigated. We demonstrated that both iodo and chloro substituents at indolyl C3 position act as temporary blocking groups to allow the formation of 2-arylindoles through a direct desulfitative arylation, followed by *in-situ* dehalogenation. While, from 3-bromoindole derivatives, 2-aryl-3-bromoindoles were obtained without debromination, and could be converted into 2,3-diarylindoles through a second palladium coupling, which are both of interest as potential intermediates in the synthesis of bioactive molecules.

Introduction

The 2-arylindoles derivatives are an important class of molecules because this motif is found in plenty of natural products and synthetic pharmaceuticals. As examples, Kenpaullone, which contains a bromine substituent at the C5 position, displays inhibition of Cyclin-Dependent Kinase (CDK) activity.¹ Rucaparib, a fluoroindole derivative, is a drug in Phase II for the treatment of patients with ovarian cancers.² Diaplasinin is an anti-coagulant and Bazedoxifene is a selective estrogen receptor modulator developed by Pfizer.³

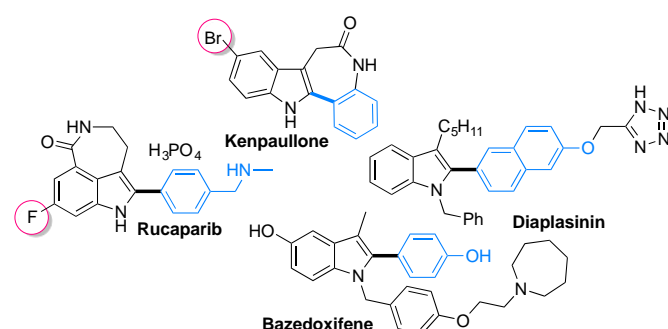


Figure 1. Pharmaceuticals containing a 2-arylindole motif.

Due to the ubiquitousness of this motif, the discovery of environmentally friendly efficient protocols with a high functional group tolerance allowing their preparation remains an important research topic. Stille,⁴ Suzuki,⁵ or Negishi⁶ Pd-catalyzed coupling reactions represent some of the most

efficient methods to prepare 2-arylindoles; however, such reactions require the previous preparation of a metallated indole or arene.

In 1985, Ohta *et al.* reported the Pd-catalyzed arylation of heteroarenes *via* a C–H bond activation and, amongst others, indole derivatives has been successfully used as substrates.⁷ Since this discovery, this methodology has proven to be a very powerful tool for a simpler and eco-friendly access to a very wide variety of arylated heterocycles, as it saves synthetic steps (*i.e.*, no preparation of metallated derivatives) and as the major by-products of the reaction are a base associated to HX.⁸ Several examples of Pd-catalyzed direct arylations of indole derivatives using aryl halides as coupling partners have been reported in recent years.⁹ Different coupling partners, such as arylboronic acids,¹⁰ aryl iodonium salts,¹¹ aryl diazonium salts,¹² arylsiloxanes,¹³ carboxylic acids,¹⁴ sodium sulfinates,¹⁵ acid sulfinates,¹⁶ or even simple arenes through a double C–H activation,¹⁷ have been successfully employed in Pd-catalyzed direct C2-arylation of indoles. Among these diverse protocols, only a few of them are tolerant towards the C–Br bonds.

Chemoselective transformations allowing sequential orthogonal transformations, especially involving sequential C–H bond activations,¹⁸ has become a very promising synthetic strategy for the straightforward synthesis of complex structures.¹⁹ As example of chemoselective C2-arylation of indoles, Sanford and co-workers reported the use of bis(4-bromophenyl)iodonium tetrafluoroborate to allow the synthesis of C2-arylated indoles, without the cleavage of the C–Br bond (Figure 1.a).^{11a} In 2012, Deng, Luo *et al.* reported a chemoselective desulfitative direct arylation of *N*-methylindole using sodium 4-bromobenzenesulfinate (Figure 1.b).¹⁵ The reaction only involved the sulfinate function and the bromine was untouched. On the other hand, Wang and *al.* extended this coupling to 4-bromobenzenesulfinic acid in acidic conditions and microwave heating (Figure 1c).¹⁶

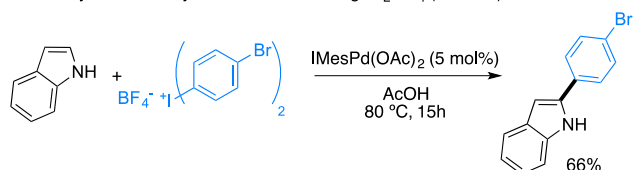
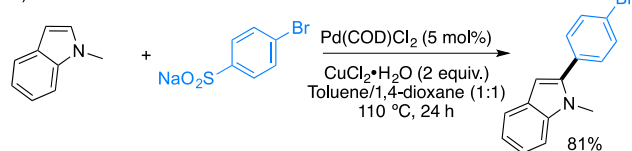
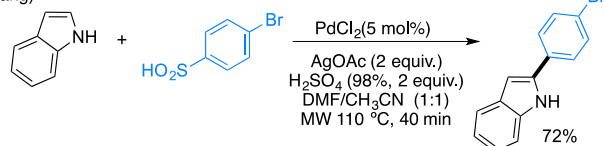
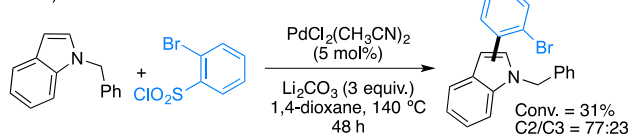
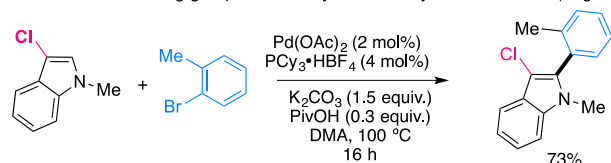
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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

a. Pd-catalyzed C–H arylation of indoles using Ar_2BF_4 (Sanford)^[11a]b. Pd-catalyzed desulfitative C–H arylation of indoles using ArSO_2Na (Deng and Luo)^[15]c. Pd-catalyzed desulfitative C–H arylation of a NH-free indole using ArSO_2H (Wang)^[16]d. Pd-catalyzed desulfitative C–H arylation of indoles using ArSO_2Cl (Soulé and Doucet)^[27]e. Chlorine as blocking group in Pd-catalyzed C–H arylation of indoles (Fagnou)^[28]

f. Halogen as (traceless)-blocking group in Pd-catalyzed desulfitative C–H arylation of indoles (This work)

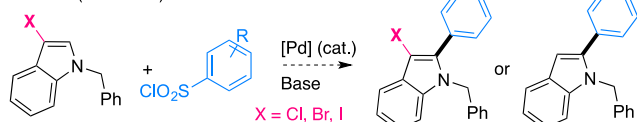


Figure 2. Palladium-catalyzed chemoselective direct arylation of indoles

During the last decade, benzenesulfonyl chloride coupling partners have been used for the direct arylation of benzoquinoline,²⁰ azoles,²¹ thiophenes,²² (benzo)furans²³ and pyrroles.²⁴ Recently, we reported on Pd-catalyzed chemoselective direct desulfitative arylation of heteroarenes using (poly)halobenzenesulfonyl chlorides,²⁵ which allowed sequential arylations.²⁶ It is important to note that in such couplings, even C–I bonds were tolerated by the optimized conditions. However, when we applied our reaction conditions to the desulfitative arylation of indoles, using 2-bromobenzenesulfonyl chloride, a mixture of C2 and C3 arylated products was obtained (Figure 1.d).^{24b, 27} Fagnou and coworkers have used 3-chloro-1-methylindole with aryl bromides as starting materials in Pd-catalyzed direct indole C2-arylation (Figure 1.e).²⁸ The chlorine atom plays the role of blocking group to overcome the regioselectivity issue of this direct coupling. Hence, we decided to investigate the reactivities of 3-chloro-, 3-bromo and 3-iodo-*N*-protected

indole derivatives in Pd-catalyzed desulfitative direct arylation (Figure 1.f).

Results

Using our previous optimized reaction conditions for Pd-catalyzed direct desulfitative arylation with heteroarenes – namely, 5 mol% of $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ catalyst associated to 3 equivalents of Li_2CO_3 as base in 1,4-dioxane at 140 °C over 48 h – we evaluated the reactivity of 1-benzyl-3-chloroindole in the presence of 4-nitrobenzenesulfonyl chloride (Table 1, entry 1). To our surprise, the desulfitative C2-arylation and the dechlorination of the C3 position occurred at the same time to afford directly the 2-arylindole **2** in 74% yield. The fact that no indole C3-arylation was observed suggests that the arylation occurred first followed by dehalogenation. Hence, the chlorine atom at indole C3-position acts as a trace-less blocking group. Next, we investigated the reactivity of 1-benzyl-3-bromoindole. In contrast to 3-chloroindole derivative, the C–Br bond was only partially cleaved under these reaction conditions, as the 3-bromo-2-arylindole **3** was isolated in 64% yield, although the debrominated 2-arylindole **2** was also formed in 28% yield (Table 1, entry 2). Hence, we decided to investigate a few reaction parameters in order to improve the yield in **3** (Table 1, entries 3–11). When the reaction was performed at a lower temperature of 100 °C, no reaction occurred (Table 1, entry 3). The change of solvent to diethylcarbonate (DEC) or cyclopentyl methyl ether (CPME) did not allowed to improve the yield of **3**. In addition, neat condition did not afford any desired arylated product, but only side products (Table 1, entries 4–6). The use of other palladium sources, such as $\text{Pd}(\text{OAc})_2$ or $\text{Pd}_2(\text{dba})_3$, only gave the debrominated coupling product **2** in low yields (Table 1, entries 7 and 8). The use of 0.5 equivalent of CuBr as additive also gave only the undesired product **2** in 65% yield (Table 1, entry 9). Finally, a shorter reaction time of 18 h allowed to reach a high **3**:**2** selectivity, and the desired 2-aryl-3-bromoindole **3** was isolated in 83% yield (Table 1, entry 10). A reaction time of 5 h lead to a poor yield in **3**, but without any formation of **2** (Table 1, entry 11). Finally, we evaluated the reactivity of 1-benzyl-3-iodoindole under the same reaction conditions. Similarly to the chloro substituent, an iodo substituent at indolyl C3-position acts as a trace-less blocking group. Indeed, only the dehalogenated C-2-arylated indole **2** was obtained in 84% yield (Table 1, entry 12).

In summary, we found that both Cl and I substituents at the indolyl C3 position are cleaved under our reaction conditions and play the role of temporary blocking group, allowing the regioselective C2-arylation of indoles. In contrast, 1-benzyl-3-bromoindole was arylated at C2 position without the cleavage of the C–Br bond.

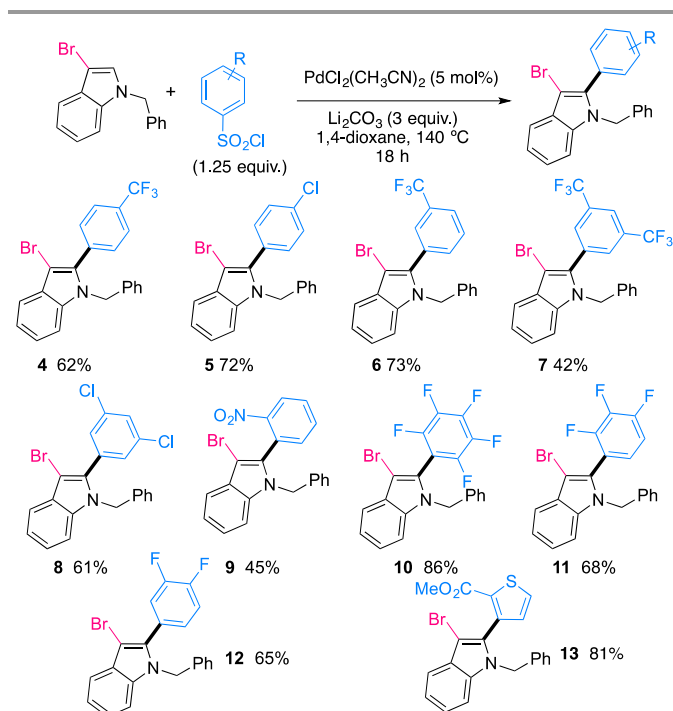
Table 1. Reactivity of 1-Benzyl-3-haloindoles in Palladium-Catalyzed Desulfative Arylation with 4-Nitrobenzenesulfonyl Chloride.

Entry	X	Modifications to conditions	Conv.	Yield of 1 , 3 or 4	Yield of 2
1	Cl	–	100%	1 , traces	73%
2	Br	–	100%	3 , 64%	28%
3	Br	100 °C	0%	0%	0%
4	Br	DEC as solvent	52%	3 , 22%	30%
5	Br	CPME as solvent	25%	3 , traces	24%
6	Br	neat, 18 h	75%	3 , traces	
7	Br	Pd(OAc) ₂	15%	3 , traces	15%
8	Br	Pd ₂ (dba) ₃	15%	3 , traces	15%
9	Br	CuBr (50 mol%)	69%	3 , traces	65%
10	Br	18 h	100%	3 , 83%	5%
11	Br	5 h	28%	3 , 28%	0%
12	I	–	100%	4 , traces	84%

i) PdCl₂(CH₃CN)₂ (5 mol%), Li₂CO₃ (3 equiv.), 1,4-dioxane, 140 °C, 48 h. DEC = diethylcarbonate; CPME = cyclopentyl methyl ether.

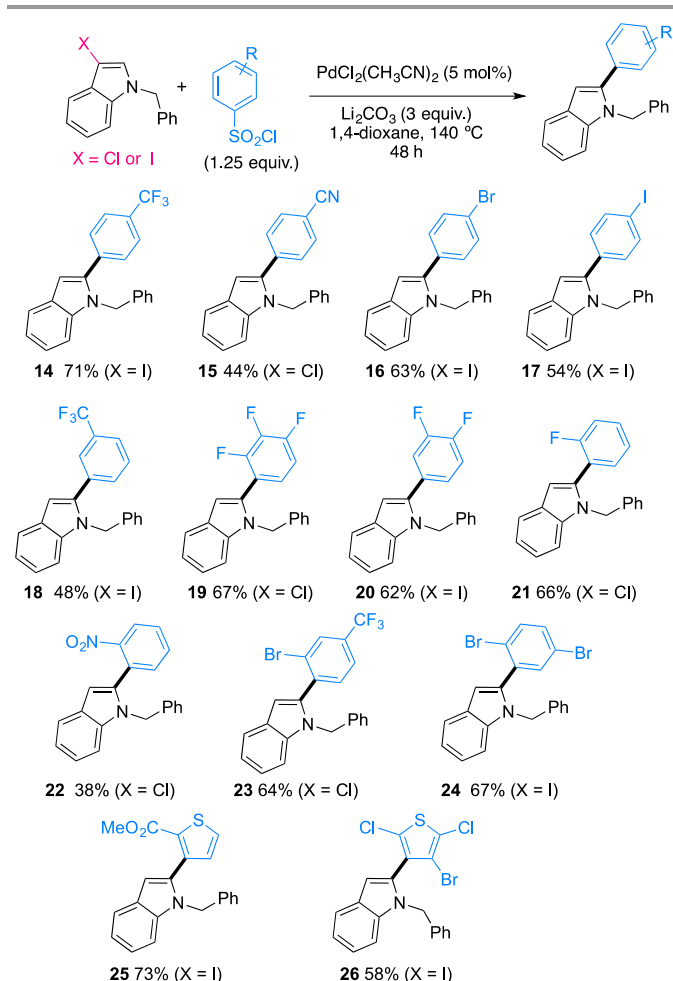
Then, we studied the scope of the benzenesulfonyl chlorides in Pd-catalyzed desulfative arylation of 1-benzyl-3-bromoindole using 5 mol% of PdCl₂(CH₃CN)₂ catalyst associated to 3 equivalents of Li₂CO₃ as base in 1,4-dioxane at 140°C over 18h (Scheme 1). Benzenesulfonyl chlorides substituted at *para*-position by an electron-withdrawing group, such as trifluoromethyl or chloro, allowed the formation of desired C2-arylated indoles **4** and **5** in 62% and 72% yields, respectively, without cleavage of the C–Br bonds. A *meta*-substituent on the benzenesulfonyl chloride has no influence on the yield, as the coupling product **6** was isolated in 73% yield. In contrast, 3,5-bis(trifluoromethyl)benzenesulfonyl chloride displayed a moderate reactivity, as the 2-arylated 3-bromoindole derivative **7** was obtained in only 42% yield. However, the coupling product **8**, resulting from the use of 3,5-dichlorobenzenesulfonyl chloride as aryl source, was isolated in 61%. The reaction seems to be sensitive to steric hindrance, as the reaction between 2-nitrobenzenesulfonyl chloride and 1-benzyl-3-bromoindole afforded the desired indole **9** in only 45% yield. Polyfluorinated molecules are ubiquitous in medicinal chemistry as well as in materials owing to fluorine atom properties (*i.e.*, electronegativity, size, lipophilicity, and electrostatic interactions), which induces a dramatic change in the molecules behavior.²⁹ Hence, we studied the reactivity of a couple of polyfluorinated benzenesulfonyl chlorides as coupling partners with 1-benzyl-3-bromoindole under the same reaction conditions.^{18c} We were pleased to find that arylation occurred again at the indolyl C2 position without the cleavage of both C–Br and C–F bonds to afford the penta-, tri- and difluorophenylindoles **10–12** in 65–86% yields. Finally, methyl 3-(chlorosulfonyl)thiophene-2-carboxylate was also

tolerated affording methyl 3-(1-benzyl-3-bromoindol-2-yl)thiophene-2-carboxylate (**13**) in 81% yield.³⁰

**Scheme 1.** Scope of Benzenesulfonyl Chlorides in Pd-Catalyzed Desulfative C2-Arylation of 1-Benzyl-3-bromoindole.

Next, we employed 1-benzyl-3-chloroindole or 1-benzyl-3-iodoindole, in which the halo substituents were used as traceless blocking groups, with a wide range of benzenesulfonyl chlorides for the one-step synthesis of 2-arylindole derivatives (Scheme 2). Overall, better yields in favor of the desired C2-arylated indole derivatives were obtained when the reaction was performed from 1-benzyl-3-iodoindole. Benzenesulfonyl chlorides substituted at *para*-position by an electron-withdrawing group such as trifluoromethyl or cyano allowed the formation of the desired C2-arylated indoles **14** and **15** in 71% and 44% yields, with the cleavage of C–X bonds. Then, we investigated the reactivity of benzenesulfonyl chlorides bearing a C–X bond. 4-bromo- and 4-iodo-benzenesulfonyl chlorides smoothly reacted with 1-benzyl-3-iodoindole to afford the C2-arylated products **16** and **17** in 63% and 54% yields, respectively. It is important to note that, unlike indolyl C–I bond, both phenyl C–Br and C–I bonds remained untouched at the end of the reactions, allowing further Pd-catalyzed orthogonal transformations. A *meta*-trifluoromethyl group on the benzenesulfonyl chloride resulted in a moderate reactivity; as from 1-benzyl-3-chloroindole, the arylated product **18** was obtained in moderate yield. Again, polyfluorinated benzenesulfonyl chlorides smoothly reacted, whatever the coupling partners, to deliver the tri-, di- and mono-fluorophenylindoles **19–21** in 62–67% yields. As seen previously, an *ortho*-substituent on the benzenesulfonyl chloride resulted in a moderate reactivity in desulfative coupling with 3-haloindoles. Indeed, the reaction between 1-benzyl-3-chloroindole and 2-nitrobenzenesulfonyl

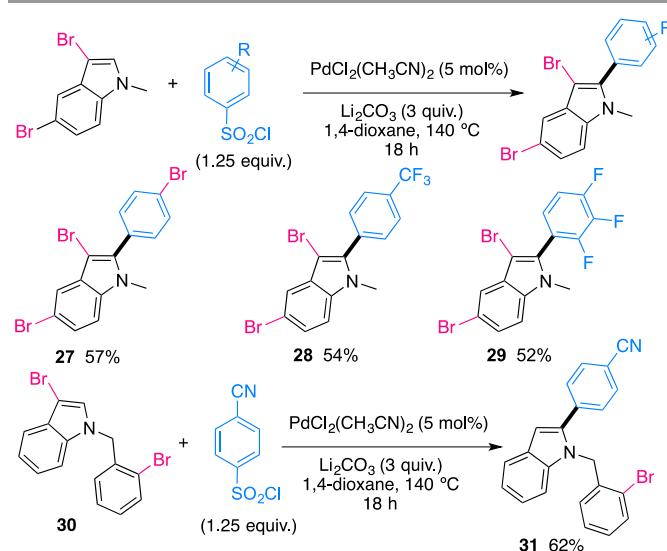
chloride afforded the arylated product **22** in only 38% yield. As one of the major advantage of the desulfitative coupling is the chemoselectivity in the presence of halo-benzenesulfonyl chlorides, we investigated other (poly)bromobenzenesulfonyl chlorides as aryl sources. The reaction between 2-bromo-4-(trifluoromethyl)benzenesulfonyl chloride and 1-benzyl-3-chloroindole afforded the 2-arylindole **23** in 64% yield, without cleavage of the C–Br bond. A similar result was observed in the case of 2,5-dibromobenzenesulfonyl chloride affording **24** in 67% yield. Thiophene-3-sulfonyl chloride derivatives were also used as coupling partners giving the heteroarenes diads **25** and **26** in 73% and 58% yields. Importantly, the thienyl C–Br and C–Cl bonds were untouched.



Scheme 2. Scope of Benzenesulfonyl Chlorides in Pd-Catalyzed Desulfitative C2-Arylation of 1-Benzyl-3-chloroindole or 1-Benzyl-3-iodoindole.

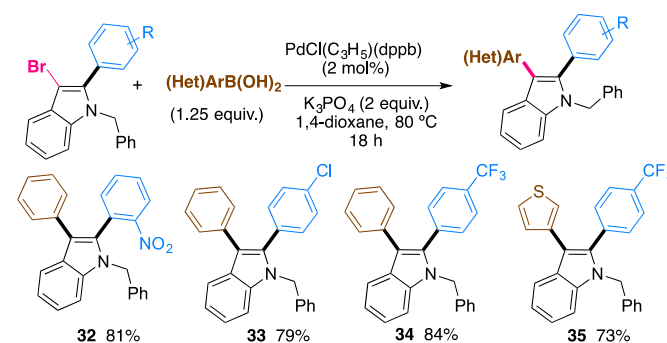
Polybrominated indoles are important building blocks in pharmaceutical synthesis, as C–Br bonds provide complementary platforms for further elaboration *via*, among others, Pd-catalyzed cross-coupling reactions. Therefore, we investigated the reactivity of polybrominated indoles in such desulfitative couplings. Under the previous optimized reaction conditions, 3,5-dibromo-1-methylindole was arylated at C2-position using 4-bromobenzenesulfonyl chloride to give the tribromoindole **27** in 57% yield, without the cleavage of the three C–Br bonds. Two other benzenesulfonyl chlorides were

also coupled to 3,5-dibromo-1-methylindole affording the 3,5-dibromoindoles **28** and **29** in 54% and 52% yields, respectively. In addition, we evaluated the reactivity of 3-bromo-1-(2-bromobenzyl)indole **30** in the presence of 4-cyanobenzenesulfonyl chloride. The 2-arylindole **31** was obtained in good yield, albeit we observed the cleavage of the indolyl C–Br bond, whereas the benzyl C–Br was untouched.



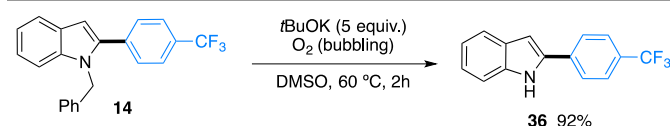
Scheme 3. Scope of Benzenesulfonyl chlorides in Pd-Catalyzed Desulfitative Arylation of 3,5-dibromo-1-methylindole and 3-Bromo-1-(2-bromobenzyl)indole.

We further demonstrated the potential of this methodology with the introduction of a second aryl group, for the two steps synthesis of 2,3-diarylindole derivatives containing two different aryl units (Scheme 4). From a mixture of 2-aryl-3-bromoindole **9** and phenylboronic acid (1.2 equivalents) in the presence of 2 mol% of a diphosphine-palladium catalyst and 2 equivalent of K_3PO_4 in dioxane at 80 °C over 18h, the 2,3-diarylindole **32** was obtained in 81% yield. Other 2,3-diarylindoles, with different substituents (*e.g.*, Cl, CF_3) on the C2-aryl group, were subjected to the same reaction conditions and allowed the formation of the desired coupling products **33** and **34** in similar yields. Finally, an heteroarylboronic acid, such as thiophen-3-ylboronic acid, was coupled with **4** to afford the 2,3-diarylindole **35** in 73% yield.



Scheme 4. Pd-Catalyzed Functionalizations of the 2-Aryl-3-bromoindole Derivatives Through Suzuki Coupling Reaction.

As a lot of natural products and pharmaceuticals contain NH-free indole motifs, we demonstrated that the *N*-benzyl substituent of indole derivative **14** could be deprotected (Scheme 5). We used slightly modified conditions described by Deaton-Rewolinski,³¹ namely large excess of *t*BuOK (5 equiv.) in DMSO at 60 °C under oxygen bubbling. Using these conditions, the indole derivative **14** was deprotected into the NH-free indole **36** in 92% yield.



Scheme 5. Debenzylation of the indole derivative **14**.

Conclusions

In summary, we reported herein on the reactivity of 3-halo-*N*-protected-indoles in Pd-catalyzed desulfative arylation using benzenesulfonyl chlorides as aryl sources. We shown that a bromo substituent at indolyl C3 position can be used as a blocking group and then used in further chemical transformation in orthogonal synthesis of 2,3-diarylindoles containing two different aryl groups. On the contrary, both indolyl chloro or iodo C3-substituents act as traceless blocking groups to regioselectively afford the dehalogenated C2-arylated indoles in good yields. A wide range of benzenesulfonyl chloride was tolerated by the optimized reaction conditions including those bearing C–Br and C–I bonds. Thanks to this chemoselectivity, this Pd-catalyzed orthogonal transformation scheme could have the potential to streamline pharmaceutical development, providing a new rapid and efficient method to discover drug candidates.

Experimental Section

General: All reactions were carried out under argon atmosphere with standard Schlenk-tube techniques. HPLC grade 1,4-dioxane was stored under argon and used without further purification. ¹H NMR spectra were recorded on Bruker GPX (400 MHz or 300 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million relative to residual chloroform (7.26 ppm for ¹H ; 77.0 ppm for ¹³C), constants were reported in Hertz. ¹H NMR assignment abbreviations were the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). ¹³C NMR spectra were recorded at 100 MHz on the same spectrometer and reported in ppm. All reagents were weighed and handled in air.

Preparation of the PdCl(C₃H₅)(dppb) catalyst:³² An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with [Pd(C₃H₅)Cl]₂ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane were added, then, the solution was stirred at room temperature for twenty minutes. The solvent was removed in vacuum. The powder was used without purification. (³¹P NMR 381 MHz, CDCl₃) δ = 19.3 (s).

General procedure for synthesis of heteroarylated heteroarenes: To a 25 mL oven dried Schlenk tube, arylsulfonyl chloride (1.25 mmol), 3-haloindole derivative (1 mmol), Li₂CO₃ (0.222 g, 3 mmol), 1,4-dioxane (2 mL) and PdCl₂(CH₃CN)₂ (12.9 mg, 0.05 mmol) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 140 °C (oil bath temperature) for 18–48 h (see tables and schemes). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the 2-arylated indoles.

1-Benzyl-2-(4-nitrophenyl)indole (2): 1-Benzyl-3-chloroindole (0.241 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **2** in 73 % (0.241 g) or 84% (0.276 g) from 1-benzyl-3-iodoindole (0.333 g, 1 mmol) yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.23 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.33–7.22 (m, 5H), 7.22–7.16 (m, 1H), 7.03 (dd, *J* = 1.9 and 7.3 Hz, 2H), 6.80 (s, 1H), 5.39 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 147.1, 139.2, 139.0, 137.5, 129.4, 129.0, 128.0, 127.6, 125.8, 123.9, 123.3, 121.2, 120.8, 110.7, 104.8, 48.1. Elemental analysis: calcd (%) for C₂₁H₁₆N₂O₂ (328.37): C 76.81, H 4.91; found: C 77.13, H 4.82.

1-Benzyl-3-bromo-2-(4-nitrophenyl)indole (3): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **3** in 83% (0.338 g) yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.28 (d, *J* = 8.7 Hz, 2H), 7.70–7.66 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.307.24 (m, 7H), 6.95–6.90 (m, 1H), 5.30 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 147.7, 137.2, 137.0, 135.6, 131.4, 131.2, 129.0, 127.7, 127.5, 125.8, 124.3, 123.7, 121.4, 120.0, 110.8, 92.9, 48.6. Elemental analysis: calcd (%) for C₂₁H₁₅BrN₂O₂ (407.27): C 61.93, H 3.71; found: C 61.69, H 3.79.

1-Benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (4): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **4** in 62% (0.267 g) yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.70–7.66 (m, 3H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.33–7.24 (m, 6H), 6.97–6.93 (m, 2H), 5.28 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 137.3, 136.8, 136.5, 134.1, 131.0, 130.9 (q, *J* = 21.9 Hz), 128.9, 127.6, 127.5, 125.9, 125.5 (q, *J* = 3.2 Hz), 124.0 (q, *J* = 271.0 Hz), 123.8, 121.2, 119.8, 110.7, 92.0, 48.4. Elemental analysis: calcd (%) for C₂₂H₁₅BrF₃N (430.27): C 61.41, H 3.51; found: C 61.28, H 3.83.

1-Benzyl-3-bromo-2-(4-chlorophenyl)indole (5): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-chlorobenzenesulfonyl chloride (0.264 g, 1.25 mmol) affords **5** in 72% (0.286 g) yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.70–7.66 (m, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.31–7.23 (m, 6H), 6.99–6.94 (m, 2H), 5.30 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 137.4, 136.9, 136.6, 135.0, 131.9, 131.7, 128.8, 127.5, 125.9, 123.4, 121.0, 120.9, 119.6, 118.5, 110.7, 91.5, 48.3. Elemental analysis: calcd (%) for C₂₁H₁₅BrClN (396.71): C 63.58, H 3.81; found: C 63.73, H 3.89.

1-Benzyl-3-bromo-2-(3-(trifluoromethyl)phenyl)indole (6): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **6** in 73% (0.314 g) yield. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.68–7.65 (m, 1H), 7.65–6.61 (m, 2H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.53 (t, *J* = 7.0 Hz, 1H), 7.28–7.21 (m, 6H), 6.94–6.88 (m, 2H), 5.26 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 137.2, 136.7, 136.4, 133.8, 131.2, 130.9 (q, *J* = 33.0 Hz), 129.0, 128.8, 127.5 (q, *J* = 3.0 Hz), 125.9, 125.5 (q, *J* = 3.0 Hz), 123.8 (q, *J* = 262.7 Hz), 123.6, 121.1, 120.9, 119.7, 118.7, 110.6, 91.9, 48.4. Elemental analysis: calcd (%) for C₂₂H₁₅BrF₃N (430.27): C 61.41, H 3.51; found: C 61.67, H 3.29.

1-Benzyl-3-bromo-2-(3,5-bis(trifluoromethyl)phenyl)indole (7): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (0.391 g, 1.25 mmol) affords **7** in 42% (0.209 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.89 (brs, 1H), 7.81 (brs, 2H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.36–7.32 (m, 2H), 7.32–7.27 (m, 1H), 7.27–7.23 (m, 3H), 6.92–6.88 (m, 2H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.2, 137.0, 134.6, 132.6, 132.1, 131.7, 130.7 (m), 129.0, 127.9, 127.2, 125.8, 124.4, 122.9 (q, $J = 262.7$ Hz), 122.3 (m), 120.0, 110.5, 92.9, 48.6. Elemental analysis: calcd (%) for $\text{C}_{23}\text{H}_{14}\text{BrF}_6\text{N}$ (498.27): C 55.44, H 2.83; found: C 55.42, H 2.81.

1-Benzyl-3-bromo-2-(3,5-dichlorophenyl)indole (8): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,5-dichlorobenzenesulfonyl chloride (0.307 g, 1.25 mmol) affords **8** in 61% (0.263 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.68–7.65 (m, 1H), 7.42 (t, $J = 2.1$ Hz, 1H), 7.29–7.26 (m, 5H), 7.26–7.24 (m, 3H), 6.94–6.90 (m, 2H), 5.28 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.2, 136.8, 135.2, 135.1, 133.3, 129.0, 128.9, 128.8, 127.7, 127.3, 126.0, 123.9, 121.2, 119.9, 110.7, 92.3, 48.5. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{14}\text{BrCl}_2\text{N}$ (431.15): C 58.50, H 3.27; found: C 58.21, H 3.14.

1-Benzyl-3-bromo-2-(2-nitrophenyl)indole (9): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **9** in 45% (0.183 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.15–8.12 (m, 1H), 7.65–7.59 (m, 3H), 7.35–7.30 (m, 1H), 7.28–7.25 (m, 3H), 7.23–7.19 (m, 3H), 6.94–6.90 (m, 2H), 5.36 (d, $J = 16.8$ Hz, 1H), 5.05 (d, $J = 16.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 149.7, 137.0, 136.5, 133.5, 132.9, 130.5, 128.7, 127.6, 127.1, 126.3, 125.7, 124.8, 123.5, 120.9, 119.6, 118.6, 110.6, 92.0, 48.8. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{15}\text{BrN}_2\text{O}_2$ (407.27): C 61.93, H 3.71; found: C 62.12, H 3.58.

1-Benzyl-3-bromo-2-(perfluorophenyl)indole (10): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2,3,4,5,6-pentafluorobenzenesulfonyl chloride (0.333 g, 1.25 mmol) affords **10** in 86% (0.388 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.68 (d, $J = 7.4$ Hz, 1H), 7.33–7.29 (m, 2H), 7.29–7.24 (m, 1H), 7.23–7.19 (m, 3H), 6.86 (ddd, $J = 1.5$, 3.1 and 5.9 Hz, 2H), 5.23 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 144.9 (md, $J = 251.2$ Hz), 142.2 (md, $J = 266.8$ Hz), 137.8 (md, $J = 251.2$ Hz), 137.1, 136.2, 128.8, 127.8, 127.0, 126.0, 124.3, 122.6, 121.1, 120.0, 110.6, 105.9 (t, $J = 18.9$ Hz), 95.7, 48.6. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{11}\text{BrF}_5\text{N}$ (452.22): C 55.78, H 2.45; found: C 55.98, H 2.38.

1-Benzyl-3-bromo-2-(2,3,4-trifluorophenyl)indole (11): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **11** in 68% (0.283 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.71–7.66 (m, 1H), 7.33–7.25 (m, 4H), 7.24–7.20 (m, 2H), 7.04 (dq, $J = 2.4$ and 5.3 Hz, 2H), 6.88 (dd, $J = 2.7$ and 5.5 Hz, 2H), 5.34 (d, $J = 16.8$ Hz, 1H), 5.16 (d, $J = 16.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 151.9 (ddd, $J = 3.9$, 10.2 and 256.3 Hz), 149.6 (ddd, $J = 3.9$, 10.2 and 256.3 Hz), 140.3 (td, $J = 14.7$ and 247.9 Hz), 136.8, 136.6, 130.2, 128.7, 127.6, 127.2, 126.7 (m), 126.0, 123.8, 121.0, 119.7, 116.1 (dd, $J = 2.8$ and 12.0 Hz), 112.4 (dd, $J = 3.2$ and 17.4 Hz), 110.6, 93.5, 48.4. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{13}\text{BrF}_3\text{N}$ (416.24): C 60.60, H 3.15; found: C 60.84, H 3.29.

1-Benzyl-3-bromo-2-(3,4-difluorophenyl)indole (12): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,4-difluorobenzenesulfonyl chloride (0.266 g, 1.25 mmol) affords **12** in 65% (0.259 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.90 (dddd, $J = 2.4$, 6.7, 9.0 and 15.5 Hz, 1H), 7.69–7.65 (m, 1H), 7.44 (dt, $J = 7.1$ and 9.3 Hz, 1H), 7.34–7.19 (m, 6H), 7.17–7.13 (m, 1H), 6.97–6.89 (m, 2H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 150.6 (dd, $J = 17.7$ and 148.8 Hz), 150.0 (dd, $J = 17.7$ and 148.8 Hz), 137.2, 136.5,

135.8, 129.8, 127.5, 127.2, 127.0 (m), 125.8, 123.6, 121.0, 119.8 (d, $J = 18.5$ Hz), 119.6, 117.5 (d, $J = 16.2$ Hz), 110.6, 91.8, 48.2. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{14}\text{BrF}_2\text{N}$ (398.25): C 63.33, H 3.54; found: C 63.67, H 3.91.

Methyl 3-(1-benzyl-3-bromoindol-2-yl)thiophene-2-carboxylate (13): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and methyl 3-(chlorosulfonyl)thiophene-2-carboxylate (0.301 g, 1.25 mmol) affords **13** in 81% (0.345 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.63–7.60 (m, 1H), 7.54 (d, $J = 5.3$ Hz, 1H), 7.51 (d, $J = 5.3$ Hz, 1H), 7.27–7.23 (m, 1H), 7.23–7.19 (m, 1H), 7.19–7.15 (m, 2H), 7.05 (d, $J = 4.9$ Hz, 1H), 6.98 (d, $J = 4.9$ Hz, 1H), 6.89 (dd, $J = 2.8$ and 5.5 Hz, 2H), 5.27 (d, $J = 16.5$ Hz, 1H), 5.15 (d, $J = 16.4$ Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 161.6, 137.4, 136.3, 135.7, 132.3, 132.0, 131.8, 130.7, 128.6, 127.4, 127.2, 126.4, 123.1, 120.6, 119.5, 110.4, 92.3, 52.3, 48.5. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{16}\text{BrNO}_2\text{S}$ (426.32): C 59.16, H 3.78; found: C 59.36, H 4.02.

1-Benzyl-2-(4-(trifluoromethyl)phenyl)indole (14): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **14** in 71% (0.249 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.15 (ddd, $J = 1.3$, 4.6 and 6.8 Hz, 1H), 8.09 (ddd, $J = 1.7$, 5.0 and 7.9 Hz, 2H), 8.03–7.98 (m, 2H), 7.75–7.70 (m, 3H), 7.69–7.62 (m, 3H), 7.48 (dd, $J = 4.7$ and 7.2 Hz, 2H), 7.17 (s, 1H), 5.28 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 140.1, 138.4, 137.8, 136.2, 129.9 (q, $J = 33.0$ Hz), 129.2, 128.8, 129.1, 127.4, 125.8, 125.5 (q, $J = 2.1$ Hz), 124.1 (q, $J = 279.8$ Hz), 122.6, 120.8, 120.5, 110.6, 103.5, 47.8. Elemental analysis: calcd (%) for $\text{C}_{22}\text{H}_{16}\text{F}_3\text{N}$ (362.26): C 75.20, H 4.59; found: C 75.64, H 4.89.

4-(1-Benzylindol-2-yl)benzonitrile (15): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.252 g, 1.25 mmol) affords **15** in 44% (0.136 g) yield. ^1H NMR (300 MHz, CDCl_3) δ (ppm) 7.70–7.63 (m, 3H), 7.51 (d, $J = 8.1$ Hz, 2H), 7.29–7.15 (m, 6H), 7.00 (d, $J = 7.2$ Hz, 2H), 6.74 (s, 1H), 5.35 (s, 2H). This is a known compound and the spectral data are identical to those reported in literature.³³

1-Benzyl-2-(4-bromophenyl)indole (16): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.319 g, 1.25 mmol) affords **16** in 63% (0.228 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.71–7.67 (m, 1H), 7.53 (d, $J = 8.5$ Hz, 2H), 7.35–7.28 (m, 4H), 7.26–7.24 (m, 1H), 7.22–7.18 (m, 2H), 7.18–7.14 (m, 1H), 7.03 (dd, $J = 2.1$ and 7.3 Hz, 2H), 6.67 (s, 1H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 140.5, 138.2, 138.0, 131.7, 131.6, 130.7, 128.8, 128.2, 127.3, 125.9, 122.4, 122.3, 120.7, 120.4, 110.5, 102.7, 47.8. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{16}\text{BrN}$ (351.37): C 69.63, H 4.45; found: C 69.27, H 4.78.

1-Benzyl-2-(4-iodophenyl)indole (17): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-iodobenzenesulfonyl chloride (0.378 g, 1.25 mmol) affords **17** in 54% (0.221 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.72 (d, $J = 8.2$ Hz, 2H), 7.70–7.68 (m, 1H), 7.32–7.24 (m, 3H), 7.21–7.13 (m, 5H), 7.02 (d, $J = 7.4$ Hz, 2H), 6.66 (s, 1H), 5.35 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 140.5, 138.2, 137.9, 137.7, 132.1, 130.8, 128.8, 128.2, 127.3, 125.8, 122.2, 120.6, 120.3, 110.5, 102.7, 93.9, 47.7. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{16}\text{IN}$ (409.27): C 61.63, H 3.94; found: C 69.89, H 4.13.

1-Benzyl-2-(3-(trifluoromethyl)phenyl)indole (18): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 3-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **18** in 48% (0.169 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.71–7.66 (m, 2H), 7.59 (dd, $J = 7.9$ and 10.2 Hz, 2H), 7.49 (t, $J = 7.7$ Hz, 1H), 7.31–7.22 (m, 5H), 7.19 (d, $J = 2.2$ and 7.3 Hz, 2H), 7.01 (d, $J = 7.1$

Hz, 2H), 6.71 (s, 1H), 5.35 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 140.0, 138.3, 137.8, 133.5, 132.2, 131.0 (q, J = 31.5 Hz), 129.0, 128.8, 128.1, 127.4, 126.0 (q, J = 3.0 Hz), 125.8, 124.6 (q, J = 3.0 Hz), 123.9 (q, J = 266.9 Hz), 122.5, 120.8, 120.4, 110.5, 103.3, 47.8. Elemental analysis: calcd (%) for $\text{C}_{22}\text{H}_{16}\text{F}_3\text{N}$ (351.37): C 75.20, H 4.59; found: C 75.59, H 4.42.

1-Benzyl-2-(2,3,4-trifluorophenyl)indole (19): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **19** in 67% (0.226 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.69 (dd, J = 1.5 and 7.7 Hz, 1H), 7.24–7.18 (m, 5H), 7.15 (t, J = 8.2 Hz, 1H), 7.07–6.98 (m, 1H), 6.98–6.92 (m, 1H), 6.9 (dd, J = 2.3 and 6.9 Hz, 2H), 6.68 (s, 1H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 151.2 (md, J = 256.3 Hz), 149.3 (md, J = 256.3 Hz), 140.2 (md, J = 256.3 Hz), 137.7, 137.4, 132.6, 128.6, 128.0, 127.3, 126.0, 125.6 (m), 122.6, 120.9, 120.3, 118.4 (dd, J = 3.8 and 12.4 Hz), 112.1 (dd, J = 4.0 and 17.9 Hz), 110.6, 104.7, 47.9. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{14}\text{F}_3\text{N}$ (337.35): C 74.77, H 4.18; found: C 74.96, H 4.36.

1-Benzyl-2-(3,4-difluorophenyl)indole (20): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 3,4-difluorobenzenesulfonyl chloride (0.266 g, 1.25 mmol) affords **20** in 62% (0.198 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.69–7.65 (m, 1H), 7.31–7.21 (m, 5H), 7.21–7.10 (m, 4H), 6.99 (d, J = 7.5 Hz, 2H), 6.63 (s, 1H), 5.34 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 150.3 (dm, J = 253.1 Hz), 150.5 (dm, J = 253.1 Hz), 139.4, 138.1, 137.7, 129.7 (t, J = 6.8 Hz), 128.9, 128.0, 127.4, 125.8, 125.3 (dd, J = 3.0 and 6.0 Hz), 122.4, 120.7, 120.4, 118.2 (d, J = 17.7 Hz), 117.4 (d, J = 17.3 Hz), 110.5, 103.0, 47.7. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{15}\text{F}_2\text{N}$ (319.35): C 78.98, H 4.73; found: C 79.24, H 5.01.

1-Benzyl-2-(2-fluorophenyl)indole (21): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-fluorobenzenesulfonyl chloride (0.243 g, 1.25 mmol) affords **21** in 66% (0.199 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.71–7.68 (m, 1H), 7.42–7.34 (m, 2H), 7.25–7.14 (m, 8H), 6.95 (d, J = 7.5 Hz, 2H), 6.69 (s, 1H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 160.2 (d, J = 250.9 Hz), 137.9, 137.6, 135.0, 132.4, 130.4 (d, J = 8.5 Hz), 128.6, 128.3, 127.1, 126.2, 124.2 (d, J = 2.8 Hz), 122.1, 120.7, 120.6, 120.1, 116.0 (d, J = 22.0 Hz), 110.6, 104.0, 47.9. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{16}\text{FN}$ (301.36): C 83.70, H 5.35; found: C 83.99, H 5.18.

1-Benzyl-2-(2-nitrophenyl)indole (22): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **22** in 38% (0.125 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.99–7.86 (m, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.57–7.51 (m, 2H), 7.37–7.33 (m, 1H), 7.25–7.12 (m, 6H), 6.92 (dd, J = 2.9 and 5.5 Hz, 2H), 6.55 (s, 1H), 5.21 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 150.0, 137.6, 137.5, 135.3, 133.5, 132.2, 129.6, 128.6, 128.0, 127.3, 126.3, 124.1, 122.4, 120.9, 120.2, 110.5, 103.3, 48.0. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_2$ (328.37): C 76.81, H 4.91; found: C 77.2, H 5.12.

1-Benzyl-2-(2-bromo-4-(trifluoromethyl)phenyl)indole (23): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-bromo-4-(trifluoromethyl)benzenesulfonyl chloride (0.404 g, 1.25 mmol) affords **23** in 64% (0.275 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.96 (s, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.3 (d, J = 7.3 Hz, 1H), 7.23 (dt, J = 0.9 and 7.1 Hz, 1H), 7.21–7.16 (m, 4H), 6.88–6.84 (m, 2H), 6.65 (s, 1H), 5.22 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.8, 137.5, 137.1, 133.1, 132.1 (q, J = 32.1 Hz), 129.8 (m), 128.6, 127.8, 127.3, 126.2, 125.4, 123.9 (m), 123.0 (q, J = 276.5 Hz), 122.5, 121.0, 120.3, 110.5,

104.0, 47.8. Elemental analysis: calcd (%) for $\text{C}_{22}\text{H}_{15}\text{BrF}_3\text{N}$ (430.26): C 61.41, H 3.51; found: C 61.75, H 3.87.

1-Benzyl-2-(2,5-dibromophenyl)indole (24): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 2,5-dibromobenzenesulfonyl chloride (0.418 g, 1.25 mmol) affords **24** in 67% (0.296 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.72 (d, J = 7.7 Hz, 1H), 7.56 (d, J = 9.3 Hz, 1H), 7.43 (s, 1H), 7.32–7.27 (m, 4H), 7.27–7.17 (m, 4H), 6.92–6.88 (m, 2H), 5.24 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.8, 137.5, 136.9, 135.9, 135.6, 134.0, 133.0, 128.5, 127.8, 127.3, 126.3, 123.8, 122.3, 121.0, 120.8, 120.1, 110.4, 103.7, 47.8. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{15}\text{Br}_2\text{N}$ (441.17): C 57.17, H 3.43; found: C 57.39, H 3.91.

1-Methyl 3-(1-benzylindol-2-yl)thiophene-2-carboxylate (25): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and methyl 3-(chlorosulfonyl)thiophene-2-carboxylate (0.301 g, 1.25 mmol) affords **25** in 73% (0.254 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.69 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 5.2 Hz, 1H), 7.28 (t, J = 7.6 Hz, 2H), 7.25–7.11 (m, 4H), 7.01 (d, J = 5.0 Hz, 1H), 6.93 (d, J = 2.8 Hz, 2H), 6.66 (s, 1H), 5.26 (s, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 161.8, 138.4, 137.9, 137.2, 134.1, 132.2, 130.3, 128.4, 127.9, 127.1, 126.3, 121.9, 120.7, 119.8, 110.4, 110.3, 103.4, 52.1, 47.7. Elemental analysis: calcd (%) for $\text{C}_{21}\text{H}_{17}\text{NO}_2\text{S}$ (347.43): C 72.60, H 4.93; found: C 72.99, H 5.13.

1-Benzyl-2-(4-bromo-2,5-dichlorothiophen-3-yl)indole (26): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-bromo-2,5-dichlorothiophene-3-sulfonyl chloride (0.301 g, 1.25 mmol) affords **26** in 58% (0.253 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.77 (d, J = 7.7 Hz, 1H), 7.36 (dd, J = 1.6 and 7.5 Hz, 1H), 7.32–7.20 (m, 5H), 7.02–6.98 (m, 2H), 6.70 (s, 1H), 5.32 (d, J = 16.3 Hz, 1H), 5.23 (d, J = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.2, 137.1, 131.3, 130.5, 128.5, 127.8, 127.7, 127.4, 126.5, 123.6, 122.6, 121.2, 120.1, 113.4, 110.5, 105.4, 48.0. Elemental analysis: calcd (%) for $\text{C}_{19}\text{H}_{12}\text{BrCl}_2\text{NS}$ (437.17): C 52.20, H 2.77; found: C 52.45, H 3.14.

3,5-Dibromo-2-(4-bromophenyl)-1-methylindole (27): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.319 g, 1.25 mmol) affords **27** in 57% (0.253 g) yield. ^1H NMR (400 MHz, C_6D_6) δ (ppm) 8.11 (s, 1H), 7.45 (dd, J = 2.0 and 8.7 Hz, 1H), 7.35 (d, J = 8.3 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 6.66 (d, J = 8.7 Hz, 1H), 2.73 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 138.2, 136.2, 132.7, 132.2, 129.7, 129.0, 126.6, 123.9, 122.8, 114.9, 112.0, 90.2, 31.2. Elemental analysis: calcd (%) for $\text{C}_{15}\text{H}_{10}\text{Br}_3\text{N}$ (443.96): C 40.58, H 2.27; found: C 40.75, H 2.12.

3,5-Dibromo-1-methyl-2-(4-(trifluoromethyl)phenyl)indole (28): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **28** in 54% (0.234 g) yield. ^1H NMR (400 MHz, C_6D_6) δ (ppm) 8.02 (s, 1H), 7.38–7.31 (m, 3H), 6.98 (d, J = 7.8 Hz, 2H), 6.56 (d, J = 8.9 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 137.7, 136.3, 134.1, 131.5, 130.8 (q, J = 29.8 Hz), 129.6, 126.9, 125.8 (q, J = 4.0 Hz), 122.9, 120.6 (q, J = 259.1 Hz), 115.0, 112.1, 90.7, 31.5. Elemental analysis: calcd (%) for $\text{C}_{16}\text{H}_{10}\text{Br}_2\text{F}_3\text{N}$ (433.07): C 44.38, H 2.33; found: C 44.19, H 2.61.

3,5-Dibromo-1-methyl-2-(2,3,4-trifluorophenyl)indole (29): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **29** in 52% (0.218 g) yield. ^1H NMR (400 MHz, C_6D_6) δ (ppm) 7.97 (s, 1H), 7.32 (dd, J = 1.9 and 8.7 Hz, 1H), 6.52 (d, J = 8.7 Hz, 1H), 6.50–6.45 (m, 1H), 6.34 (ddt, J = 1.9, 7.1 and 9.3 Hz, 1H), 2.65 (s,

3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 152.4 (md, $J = 249.1$ Hz), 150.0 (md, $J = 249.1$ Hz), 141.0 (td, $J = 8.0$ and 252.8 Hz), 136.2, 131.7, 129.4, 127.3 (m), 127.1, 123.0, 116.4 (dd, $J = 4.8$ and 12.1 Hz), 115.0, 112.8 (dd, $J = 3.6$ and 17.5 Hz), 112.1, 91.9, 31.0. Elemental analysis: calcd (%) for $\text{C}_{15}\text{H}_8\text{Br}_2\text{F}_3\text{N}$ (419.04): C 42.99, H 1.92; found: C 43.26, H 2.27.

3-Bromo-1-(2-bromobenzyl)indole (30): To a solution of 3-bromoindole (1 g, 5.15 mmol, 1 equiv.) in DMF (10 ml) was added in small portions 60% oil NaH (0.25 g, 6.43 mmol, 1.25 mmol) at 0 °C. The resulting mixture was stirred at room temperature over 1 h before adding 2-bromobenzyl bromide (1.60 g, 6.43 mmol, 1.25 mmol). Then, the mixture was stirred at room temperature for 4 h. The resulting solution was poured in NH_4Cl aqueous solution (100 ml). The mixture was extracted with three 100-ml. portions of diethyl ether, and each ether layer was washed with three 50-ml. portions of water. The combined ether layers were dried over MgSO_4 , and the solvent was removed under slightly reduced pressure. The crude mixture was purified by silica column chromatography to afford **30** in 89% yield (1.87 g). ^1H NMR (400 MHz, C_6D_6) δ (ppm) 7.76 (d, $J = 7.9$ Hz, 1H), 7.26 (dd, $J = 1.6$ and 7.7 Hz, 1H), 7.12 (dd, $J = 6.8$ and 8.0 Hz, 1H), 7.03 (dd, $J = 6.8$ and 8.3 Hz, 1H), 6.79 (d, $J = 8.3$ Hz, 1H), 6.59–6.49 (m, 2H), 6.47 (s, 1H), 6.14 (dd, $J = 1.9$ and 7.5 Hz, 1H), 4.70 (s, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 136.9, 136.6, 133.1, 129.5, 129.0, 127.9, 123.8, 122.5, 121.4, 120.2, 110.5, 91.4, 50.5. Elemental analysis: calcd (%) for $\text{C}_{15}\text{H}_{11}\text{Br}_2\text{N}$ (365.06): C 49.35, H 3.04; found: C 49.59, H 2.81.

4-(1-(2-Bromobenzyl)indol-2-yl)benzonitrile (31): 3-bromo-1-(2-bromobenzyl)indole (**30**) (0.365 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.252 g, 1.25 mmol) affords **31** in 62% (0.240 g) yield. ^1H NMR (400 MHz, C_6D_6) δ (ppm) 7.71 (d, $J = 7.9$ Hz, 1H), 6.32–7.29 (m, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.1 (dd, $J = 6.9$ and 8.5 Hz, 1H), 6.92 (d, $J = 8.3$ Hz, 2H), 6.82 (d, $J = 8.6$ Hz, 1H), 6.77 (d, $J = 8.3$ Hz, 2H), 6.67–6.54 (m, 2H), 6.54 (s, 1H), 6.46–6.40 (m, 1H), 5.00 (s, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 140.0, 139.5, 137.3, 136.7, 133.4, 132.7, 129.5, 129.1, 129.0, 128.5, 128.0, 124.0, 122.1, 121.8, 121.7, 118.9, 112.3, 111.2, 105.0, 49.0. Elemental analysis: calcd (%) for $\text{C}_{22}\text{H}_{15}\text{BrN}_2$ (387.28): C 68.23, H 3.90; found: C 68.37, H 4.15.

1-Benzyl-2-(2-nitrophenyl)-3-phenylindole (32): The reaction of 1-benzyl-3-bromo-2-(2-nitrophenyl)indole (**9**) (0.204 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80 °C over 15 h in 1,4-dioxane (1 mL) in the presence of $\text{PdCl}(\text{C}_3\text{H}_5)(\text{dppb})$ (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **32** in 81% (0.164 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.98 (dd, $J = 1.8$ and 7.8 Hz, 1H), 7.81 (d, $J = 7.8$ Hz, 1H), 7.55–5.45 (m, 2H), 7.34–7.17 (m, 12H), 7.00–6.97 (m, 2H), 5.39 (d, $J = 16.7$ Hz, 1H), 5.08 (d, $J = 16.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 150.3, 137.4, 134.5, 134.1, 132.6, 132.3, 129.7, 129.4, 128.6, 128.3, 127.3, 127.1, 127.0, 126.3, 126.0, 124.4, 122.8, 120.5, 119.9, 117.0, 110.4, 102.9, 48.0. Elemental analysis: calcd (%) for $\text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_2$ (404.47): C 80.18, H 4.98; found: C 80.35, H 5.17.

1-Benzyl-2-(4-chlorophenyl)-3-phenylindole (33): The reaction of 1-benzyl-3-bromo-2-(4-chlorophenyl)indole (**5**) (0.198 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80 °C over 15 h in 1,4-dioxane (1 mL) in the presence of $\text{PdCl}(\text{C}_3\text{H}_5)(\text{dppb})$ (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **33** in 79% (0.156 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.81 (dd, $J = 1.7$ and 7.5 Hz, 1H), 7.32–7.28 (m, 4H), 7.28–7.19 (m, 7H), 7.23–7.18 (m, 2H), 7.16 (d, $J = 8.5$ Hz, 2H), 7.00 (dd, $J = 2.1$ and 7.4 Hz, 2H),

5.38 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.9, 137.2, 136.5, 135.8, 134.8, 134.3, 132.3, 130.3, 129.9, 129.3, 128.8, 128.7, 128.3, 127.3, 126.0, 125.8, 122.7, 120.6, 119.8, 110.5, 47.6. Elemental analysis: calcd (%) for $\text{C}_{27}\text{H}_{20}\text{ClN}$ (393.91): C 82.33, H 5.12; found: C 82.58, H 5.29.

1-Benzyl-3-phenyl-2-(4-(trifluoromethyl)phenyl)indole (34): The reaction of 1-benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (**4**) (0.215 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80 °C over 15 h in 1,4-dioxane (1 mL) in the presence of $\text{PdCl}(\text{C}_3\text{H}_5)(\text{dppb})$ (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **34** in 84% (0.180 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.81 (d, $J = 7.7$ Hz, 1H), 7.53 (d, $J = 7.8$ Hz, 2H), 7.35 (d, $J = 8.8$ Hz, 2H), 7.32–7.29 (m, 4H), 7.28–7.24 (m, 5H), 7.24–7.18 (2H), 7.01 (d, $J = 7.4$ Hz, 2H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.8, 137.3, 136.0, 134.5, 133.3 (q, $J = 34.7$ Hz), 131.2, 130.0, 128.8, 128.4, 128.1, 127.4, 127.3, 126.0, 125.9, 125.3 (q, $J = 1.8$ Hz), 123.6 (q, $J = 275.1$ Hz), 123.0, 120.7, 119.9, 116.8, 110.5, 47.7. Elemental analysis: calcd (%) for $\text{C}_{28}\text{H}_{20}\text{F}_3\text{N}$ (427.47): C 78.67, H 4.72; found: C 78.98, H 4.49.

1-Benzyl-3-(thiophen-3-yl)-2-(4-(trifluoromethyl)phenyl)indole (35): The reaction of 1-benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (**4**) (0.215 g, 0.5 mmol), thiophen-3-ylboronic acid (0.077 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80 °C over 15 h in 1,4-dioxane (1 mL) in the presence of $\text{PdCl}(\text{C}_3\text{H}_5)(\text{dppb})$ (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **35** in 73% (0.158 g) yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.87 (d, $J = 7.2$ Hz, 1H), 7.59 (d, $J = 8.2$ Hz, 2H), 7.4 (d, $J = 8.2$ Hz, 2H), 7.30–7.22 (m, 7H), 7.16 (d, $J = 3.1$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 2H), 6.94 (d, $J = 5.2$ Hz, 1H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 137.7, 137.2, 136.0, 135.7, 134.6, 131.2, 130.3 (q, $J = 32.1$ Hz), 128.8, 128.6, 127.4, 125.9, 125.8, 125.3 (m), 125.0, 123.9 (q, $J = 279.5$ Hz), 123.0, 121.7, 120.7, 120.0, 111.8, 110.5, 47.7. Elemental analysis: calcd (%) for $\text{C}_{26}\text{H}_{18}\text{F}_3\text{NS}$ (433.49): C 72.04, H 4.19; found: C 71.89, H 3.96.

2-(4-(Trifluoromethyl)phenyl)indole (36): 1-Benzyl-2-(4-(trifluoromethyl)phenyl)indole (**14**) (0.181 g, 0.5 mmol) was dissolved in DMSO (5 mL) and added to a flame-dried flask. While stirring the solution at room temperature, $t\text{BuOK}$ (0.280 g, 2.5 mmol) was added. The solution was heated at 60 °C, then oxygen was then bubbled into the solution over 2 h. The reaction was quenched with saturated ammonium chloride. The product was extracted three times with EtOAc. The organics were combined, dried over Na_2SO_4 and concentrated. The crude mixture was purified on silica gel to afford the product **36** in 92% (0.120 g) yield. ^1H NMR (400 MHz, d^6 -DMSO) δ (ppm) 11.72 (br, 1H), 8.07 (d, $J = 8.3$ Hz, 2H), 7.81 (d, $J = 8.3$ Hz, 2H), 7.57 (d, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 8.2$ Hz, 1H), 7.17–7.13 (m, 1H), 7.07 (s, 1H), 7.05–7.01 (m, 1H). This is a known compound and the spectral data are identical to those reported in literature.³⁴

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